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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,728	01/22/2001	Habib Zaghouani	8114-005-WO-CIP.2-US	6688

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/623,728	ZAGHOUANI, HABIB	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 21-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 21-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendments received May 18, 2007 are acknowledged.

Claims 8-20 have been canceled.

Claims 1-7 and 21-28 are pending in the instant application.

Applicant's election with traverse of the disease species Multiple Sclerosis in the reply filed on May 18, 2007 is acknowledged. The traversal is on the ground(s) that the species are so closely related that there is no basis for requesting an election.

This is not found persuasive because the recited diseases have distinct etiologies and clinical courses of progression, patient populations, target autoantigens, and standard methods of treatment as was detailed in the restriction requirement.

Applicant also argues that the number of species is not unreasonably large.

This argument is not persuasive because a search for one disease, say multiple sclerosis, is unlikely to uncover relevant art that reads on clinically distinct diseases such as lupus, and insulin-dependent diabetes and therefore there is a search burden to examining all species concurrently.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-7 and 21-28 are under examination as they read on fusion proteins comprising autoantigenic polypeptides and fragments associated with the disease Multiple Sclerosis.

Information Disclosure Statement

2. Applicant's IDS received May 21, 2007 has been considered.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-3 and 21-23 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 90/09804 (of record).

The office action mailed January 2, 2004 states:

> The '804 patent teaches the use of genetically engineered Ig's, wherein the resulting Ig has Fc receptor binding region and a variable region replaced with an antigen associated with autoimmune disease wherein said Ig is to be used to down regulate the autoimmune disease (see abstract, page 5 lines 26-33, in particular).

Applicant's arguments filed May 18, 2007 have been fully considered but they are not persuasive. Applicant argues that the '804 patent teaches the use of engineered immunoglobulins to induce an immune response to an administered immunoglobulin, whereas the claimed product decreases immune responses.

This argument is not persuasive because the products disclosed by the '804 patent comprise the same structure as the fusion molecules claimed in the instant invention (see particularly from line 8 of page 5 to line 11 of page 6, from line 16 of page 10 to line 11 of page 11, and lines 14-35 of page 22).

Applicant also argues that the '804 patent does not provide adequate description of how the disclosed engineered immunoglobulins are to be used to treat autoimmune disorders.

This argument is not persuasive, because as stated above, the structure of the molecules disclosed in the '804 patent anticipates the structure of the instant claimed fusion molecules. Function is a consequence of structure, and as such if the structures are the same they will give rise to the same function, even if the function was not known at the time of the disclosure. The courts have stated "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown

property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Further, "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See also MPEP 2112.

The rejection of record is maintained.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 3, 4, 5, 24, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zanetti et al. (WO 90/09840, of record) in view of Liu et al. (International Immunology, 1995, 7:1255-1263).

Zanetti et al. disclose genetically engineered immunoglobulins comprising antigens associated with autoimmune diseases (see entire document, particularly the abstract and from line 8 of page 5 to line 11 of page 6, from line 16 of page 10 to line 11 of page 11, and lines 14-35 of page 22). Note that the exemplified constructs of Zanetti et al. comprise a human IgG Fc domain and thus are capable of undergoing Fc receptor mediated endocytosis, and that Zanetti et al. specifically discuss the importance of an intact Fc domain for targeting their constructs to Fc receptor expressing cells (see particularly lines 18-25 of page 5) . It is further disclosed that their constructs are to be used to induce tolerance, which means that the immune response to the autoantigen has been downregulated (see particularly the abstract, lines 31-35 of page 5 and lines 21-27 of page 22). These teachings differ from the instant claimed invention in that

Zanetti et al. do not disclose the specific autoimmune disease Multiple Sclerosis (MS), nor do they disclose the well known MS target autoantigen myelin basic protein (MBP).

Liu et al. teach TCR agonist peptides of MBP that induce tolerance upon administration in the mouse EAE model of MS (see entire document, particularly the abstract).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to replace the antigen of Zanetti et al. with the MBP agonist peptides disclosed by Liu et al. Motivation to do so comes from the fact that the products of Zanetti et al. and Liu et al. are both taught for use in inducing tolerance, and the fact that placing the MBP agonist of Lui et al. into a Zanetti-type Ig construct would provide a targeting mechanism that would direct the MBP peptide to Fc receptor expressing cells

7. Claims 1, 3, 4, 6, 24, 25, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zanetti et al. (WO 90/09840, of record) in view of Karpus et al. (Journal of Neuroscience Research, 1996, 45:410-423).

Zanetti et al. disclose genetically engineered immunoglobulins comprising antigens associated with autoimmune diseases (see entire document, particularly the abstract and from line 8 of page 5 to line 11 of page 6, from line 16 of page 10 to line 11 of page 11, and lines 14-35 of page 22). Note that the exemplified constructs of Zanetti et al. comprise a human IgG Fc domain and thus are capable of undergoing Fc receptor mediated endocytosis, and that Zanetti et al. specifically discuss the importance of an intact Fc domain for targeting their constructs to Fc receptor expressing cells (see particularly lines 18-25 of page 5) . It is further disclosed that their constructs are to be used to induce tolerance, which means that the immune response to the autoantigen has been downregulated (see particularly the abstract, lines 31-35 of page 5 and lines 21-27 of page 22). These teachings differ from the instant claimed invention in that Zanetti et al. do not disclose the specific autoimmune disease Multiple Sclerosis (MS), nor do they disclose the well known MS target autoantigen proteolipid protein (PLP).

Karpus et al. teach TCR agonist peptides of PLP that induce tolerance upon administration in the mouse EAE model of MS (see entire document, particularly the abstract).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to replace the antigen of Zanetti et al. with the PLP agonist peptides disclosed by Karpus et al. Motivation to do so comes from the fact that the products of Zanetti et al. and Karpus et al. are both taught for use in inducing tolerance, and the fact that placing the PLP agonist of Karpus et al. into a Zanetti-type Ig construct would provide a targeting mechanism that would direct the MBP peptide to Fc receptor expressing cells

8. Claims 7 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zanetti et al. (WO 90/09840, of record) in view of Liu et al. (International Immunology, 1995, 7:1255-1263) in view of Karpus et al. (Journal of Neuroscience Research, 1996, 45:410-423) as applied to claims 1-6 and 21-27 above, and further in view of Elliott et al. (J. Clin. Invest., 1996, 98:1602-1612).

The teachings of Zanetti et al. in view of Liu et al. and in view of Karpus et al. have been discussed above. These teachings differ from the instant claimed invention in that they do not disclose combining peptides from MBP and PLP in to the same Ig construct.

Elliott et al. disclose that administration of a fusion protein comprising epitopes of MBP and PLP is more effective in reducing the severity of symptoms of neurodegeneration than administration the autoantigens MPB or PLP in isolation (see entire document, particularly the abstract and page 1611).

Therefore, it would have been obvious to a person of ordinary skill in the art to make an immunoglobulin fusion construct comprising epitopes of MBP and PLP. Motivation to do so comes from the fact that the epitopes in isolation are known to induce tolerance as was disclosed by Liu et al. and Karpus et al. and the disclosure by

Elliott et al. that combining epitopes from MBP and PLP results in increased efficacy of tolerance induction.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-7 and 21-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicant has claimed a genus of fusion molecules, said molecules comprising an immunoglobulin domain capable of binding to Fc receptors and an autoantigenic polypeptide which comprises a T cell receptor agonist. These fusion molecules are recited as having the intended use of alleviating symptoms associated with an autoimmune disorder, and dependent claims recite various disorders such as MS, lupus, rheumatoid arthritis, scleroderma, insulin-dependent diabetes, and ulcerative colitis. To support this genus applicant has disclosed the Ig-PLP1 construct which comprises the replacement of a CDR3 region of the immunoglobulin with amino acids 139-151 of PLP.

The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics,

sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Fri. January 5, 2001, see especially page 1106 column 3).

The instant claims do not specify how or where the autoantigen is linked to the immunoglobulin domain. As such, the structure of Ig-PLP-1 is not representative of the structure of the claimed genus since the structural constraints of the Ig-PLP-1 molecule are not limitations of the claimed genus. Further, with the exception of claims 5-7 and 26-28, the identity of the autoantigen that is to be used as part of the claimed invention is not recited and the specification does not appear to disclose a representative number of autoantigens correlated with their associated diseases. It is known in the art that recognition of specific autoantigens is indicative of a particular disease, for instance, PLP is an autoantigen in MS but is not an autoantigen in ulcerative colitis, and as such it does not seem reasonable that any one autoantigen would sufficiently cover all autoimmune diseases. Therefore, the breadth of the instant claimed invention does not specify what autoantigens are to be used or how they are to be joined to an immunoglobulin moiety.

In University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398, the court noted:

"A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene (in the instant case, a peptide) does, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes (peptides) may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material."

The court has also noted that "Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Id. at 1566, 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). Also see Enzo-Biochem v. Gen-Probe 01-1230 (CAFC 2002).

As discussed above, the disclosed species is not representative of the claimed genus and the correlation between the recited structural features and functional properties does not appear to be adequately disclosed.

Therefore, it appears that the broad genus of fusion constructs claimed by applicant lacks adequate written description and as such a skilled artisan would reasonably conclude that applicant was not in possession of the claimed genus of fusion constructs at the time the application was filed.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-7 and 21-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 19 of copending Application No. 11/612,773 in view of Elliott et al. (J. Clin. Invest., 1996, 98:1602-1612).

The copending claim recites a fusion molecule wherein the CDR of an immunoglobulin has been replaced with a T cell receptor agonist specific for MS.

Elliott et al. disclose that MBP and PLP are the dominant autoantigens in MS, and that a fusion comprising epitopes from MBP and PLP is more efficacious in treating MS that either autoantigen alone (see entire document, particularly the abstract and page 1611).

As such, a skilled artisan would have been motivated to make Ig constructs comprising agonists from MBP and PLP because they are the dominant autoantigens recognized by autoreactive T cells in MS and because fusion constructs comprising agonists from both autoantigens has increased efficacy in inducing tolerance and lessening disease severity as taught by Elliott et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 1-4, 6, 21-25, and 27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 11/619,568. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims anticipate the instant claimed invention. Specifically, the copending claims recite an immunoglobulin comprising the substitution of an epitope of PLP, a known autoantigen in MS, for a CDR region of the immunoglobulin, and thus are of narrower scope than the breadth of the instant claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted that the elected invention is presently limited to the elected species of MS. However, given that examination of additional species is possible based upon the

allowability of generic claims, and given the goal of compact prosecution, claims in a copending application have been found that appear to read on a species not presently elected. Therefore, a rejection based upon the copending application has been set forth to advance prosecution.

14. Claims 1-4 and 21-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-60 of copending Application No. 10/510,411. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims recite fusion constructs comprising an immunoglobulin wherein a CDR region has been replaced with a diabetes-specific epitope of insulin or GAD. Since the copending claims recite specific autoantigens and limit the structure of the claimed fusion product by specifying how the autoantigen and immunoglobulin are linked, the copending claims anticipate the breadth of the instant claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

15. Claims 4, 24, and 25 are objected to for the recitation of "lupis" rather than the proper spelling "lupus".

16. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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